METHOD FOR DETERMINING THE DISTRIBUTION VOLUME OF A BLOOD COMPONENT DURING AN EXTRACORPOREAL BLOOD TREATMENT AND APPARATUS FOR IMPLEMENTING THE METHOD

The present invention relates to a method for determining the distribution volume of a blood component in the body of an organism, particularly the urea distribution volume, during an extracorporeal blood treatment. In

5 addition, the present invention relates to an apparatus for determining the distribution volume of a blood component in the body of an organism during an extracorporeal blood treatment in conjunction with a device for the extracorporeal blood treatment.

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An essential task of the human kidneys is the separation of substances, usually eliminated with urine, from the blood, and the regulation of the water and electrolyte excretion. Hemodialysis represents a treatment method to

15 compensate for dysfunctions of the kidneys with respect to the removal of substances usually eliminated with urine, and the adjustment of the electrolyte concentration in the blood.

20 During hemodialysis, the blood is conducted in an extracorporeal circuit through the blood chamber of a dialyzer, the blood chamber being separated from a dialyzing-fluid chamber by a semipermeable membrane. A dialyzing fluid containing the blood electrolytes in a

25 specific concentration flows through the dialyzing-fluid chamber. The substance concentration (cd) of the dialyzing fluid corresponds to the concentration of the blood of a healthy individual. During the treatment, the blood of the patient and the dialyzing fluid are

376269   1

conducted past both sides of the membrane, generally in counterflow with a predefined flow rate(Qb and Qd, respectively). The substances usually eliminated with urine diffuse through the membrane from the blood chamber into the chamber for dialyzing fluid, while at the same time, electrolytes present in the blood and in the dialyzing fluid diffuse from the chamber of higher concentration to the chamber of lower concentration. The substance exchange can be additionally influenced by applying a trans-membrane pressure.

To permit optimization of the blood-treatment process, the determination of parameters for the hemodialysis during the extracorporeal blood treatment (in-vivo) is necessary. Of interest is the value for the exchange efficiency of the dialyzer, which is represented by the so-called "clearance" or "dialysance D".

Designated as clearance for a specific substance K is that virtual (calculated) blood volume which is completely freed of a specific substance per minute under defined conditions in the dialyzer. The dialysance D is a further concept for determining the performance of a dialyzer, in which the concentration of the eliminated substance in the dialyzing fluid is taken into account. In addition to these parameters for describing the performance of the dialyzer, other parameters are also important, such as the values for the aqueous component of the blood, the blood volume and the blood input concentration, etc.

The mathematical quantification, using measuring techniques, of the blood-purification process and the determination of the aforesaid parameters of the dialysis are relatively complex. With respect to the computational

fundamentals, reference is made to J. A. Sargent, F. A. Gotch: *"Principles and Biophysics of Dialysis"* in: *Replacement of Renal Function by Dialysis*, C. Jacobs, C. M. Kjellstrand, K. M. Koch, J. F. Winchester (editor), Kluwer Academie Publisher, Dordrecht, 1996.

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The dialysance, i.e. the clearance can be determined as follows for a given electrolyte, e.g. sodium, at an ultra-filtration rate of zero. The dialysance D is equal to the relationship between the mass transport on the blood side for this electrolyte (Q_b x (cbi-cbo)) and the concentration difference of this electrolyte between the blood and the dialyzing fluid at the respective input of the dialyzer (cbi-cdi).

$$D = Qb \bullet \frac{cbi - cbo}{cbi - cdi} \qquad (1)$$

For reasons of mass balance, the following is applicable:

$$Qb \bullet (cbi - cbo) = -Qd \bullet (cdi - cdo) \qquad (2)$$

Following from the two equations (1) and (2) indicated above is:

$$D = -Qd \bullet \frac{cdi - cdo}{cbi - cdi} \qquad (3)$$

In this context, in (1) through (3):

Qb = effective flow of blood
Qd = flow of dialyzing fluid
cb = substance concentration in the blood
cd = substance concentration in the dialyzing fluid
i = input of the dialyzer

o = output of the dialyzer

The effective blood flow is the flow of the blood component in which the substances to be removed are dissolved, i.e. it relates to the (aqueous) solution volume for this substance. Depending on the substance, it can be the plasma water flow or the blood serum flow, i.e. the entire water content in the whole blood. If the whole-blood flow Q_{vb} is ascertained, then Qb can be determined from Q_{vb} using a constant factor.

In the event that the ultrafiltration rate Qf is not equal to zero, dialysance D is calculated as follows:

$$D = \left[Qd \frac{cdo - cdi}{cbi - cdi} \right] \bullet \left[1 - \frac{Qf}{Qb} \right] + Qf \qquad (4a)$$

The diffusive component of the dialysance D_{diff} is then calculated as follows:

$$D_{diff} = \left[Qd \frac{cdo - cdi}{cbi - cdi} \right] \bullet \left[1 - \frac{Qf}{Qb} \right] \qquad (4b)$$

For ionic substances, the Gibb's Donnan coefficient must be taken into account for the blood input concentration. For this, reference is made to the article by Sargent and Gotch cited above. For the sake of simplicity, this correction factor is omitted in the following.

The German patent DE 39 38 662 C2 (EP 0 428 927 A1) describes a method for the in-vivo determination of parameters for the hemodialysis, in which the

dialysate-electrolyte transfer is in each case measured for two different dialysate input concentrations. Assuming that the blood input concentration is constant, according to the known method, the dialysance is determined in that the difference is determined between the differences of the dialyzing fluid ion concentration at the input side and the output side of the dialyzer at the instant of the first and second measurement, this is divided by the difference of the dialyzing fluid ion concentration at the input side at the instant of the first measurement and of the second measurement and is multiplied by the dialyzing-fluid flow.

To be able to make a statement about the dialyzing dosage for the hemodialysis, the so-called "Kt/V" parameter is of particular interest. To calculate this parameter, the product of the clearance K and the treatment time t is formed, and is divided by the distribution volume V of the substance to be removed, usually urea.

The treatment time is predefined and therefore known. The clearance for the type of dialyzer used can be gathered from tables, or else can be ascertained online (DE 39 38 662 C2). In principle, the distribution volume of a substance can be determined using a normal dilution measurement in which an exactly measured marker fluid is injected into the patient and its uniform concentration in the blood is measured after a sufficient distribution time. However, this proves to be too costly for a routine process which must be used, for example, three times per week.

Therefore, the distribution volume V is usually ascertained with empirical estimation formulas, into

which parameters are entered such as the body size and the weight of the patient to be treated. The value ascertained for V is admittedly very imprecise.

5   A method is known from WO 98/55166 for determining the mass of a constituent such as urea in the blood, in which the concentration of the constituent in the dialyzing fluid is measured downstream of the dialyzer during the treatment. The mass of the constituent is determined from
10   the change in the concentration as a function of time. The distribution volume should be calculated from the mass of the constituent. It is disadvantageous that the distribution volume is not determined continually, but rather only at the end of a treatment segment.

15   The object of the present invention is to specify a method which allows rapid and automated determination of the distribution volume of a blood component in the body of an organism during an extracorporeal blood treatment.
20   A further objective underlying the present invention is to provide an apparatus for determining the distribution volume of a blood component in the body of an organism.

This objective is achieved according to the present
25   invention by the features specified in Patent Claims 1 and 10, respectively.

Determination of the distribution volume of a blood component in the body of an organism during an
30   extracorporeal blood treatment is based on the change in a physical or chemical characteristic of the dialyzing fluid in the dialyzing-fluid path during the blood treatment and the measurement of the physical or chemical characteristic of the dialyzing fluid downstream of the

dialyzer. The physical or chemical characteristic of the
dialyzing fluid is altered in the dialyzing-fluid path
upstream from the dialyzer. In this context, the physical
or chemical characteristic should be adjusted to

5   physiologically tenable values.

If the change in the characteristic upstream of the
dialyzer is known, it is possible to dispense with this
measurement. Otherwise the characteristic is measured not

10   only downstream, but also upstream of the dialyzer.

The change in the concentration of the blood component in
the blood as a function of time is determined from the
physical or chemical characteristic of the dialyzing

15   fluid downstream of the dialyzer. The distribution volume
of the substance in the body of an organism is then
inferred from the change in the concentration of the
blood component in the blood over time.

20   The physical or chemical characteristic of the dialyzing
fluid upstream and downstream of the dialyzer is
advantageously the concentration of a substance in the
dialyzing fluid upstream and downstream of the dialyzer
(dialyzing fluid input concentration and output

25   concentration cdi, cdo). A deviation in the dialyzing
fluid input concentration from the blood input
concentration cbi leads to a change in the blood input
concentration cbi at the dialyzer, since the measured
substance shifts to or from the blood side. The

30   distribution volume of this substance in the blood is
then inferred from the change in the blood input
concentration as a function of time.

To determine the distribution volume of sodium in the blood, preferably the conductivity of the dialyzing fluid is measured as a physical or chemical characteristic. The known conductivity sensors can be used for this purpose.

The urea distribution volume can be inferred from the sodium distribution volume, since the urea distribution volume corresponds essentially to the sodium distribution volume.

After the urea distribution volume is determined, the so-called "Kt/V" parameter can be calculated, in doing which the clearance K can either be ascertained according to the method known from DE 39 38 662 C2, or gathered from corresponding tables for the individual types of dialyzer.

In calculating the distribution volume V, the starting point is initially the following mass balance equation:

$$\int\limits_{t}^{t+\Delta t} Qd * cdi(t')dt' - \int\limits_{t}^{t+\Delta t} (Qd + Qf) * cdo(t')dt' = V(t+\Delta t) * cbi(t+\Delta t) - V(t) * cbi(t) \quad (5)$$

Equation (5) represents how the blood concentration cbi changes on the basis of the shift of substances into or out of the blood. If equation (5) is divided by Δt and the limiting value $\Delta t \to \infty$ is then considered, then the integral mass balance according to equation (5) is converted into a differential mass balance:

$$Qd * cdi(t) - (Qd + Qf) * cdo(t) = cbi(i)\frac{dV(t)}{dt} - V(t)\frac{dcbi(t)}{dt} \quad (6)$$

Solved according to dcbi(t)/dt and with dV(t)/dt = -Qf, this yields equation (7):

$$\frac{dcbi}{dt} = \frac{Qd * cdi(t) - (Qd + Qf) * cdo(t) + Qf * cbi(t)}{V(t)} \qquad (7)$$

Equation (7) represents the basis for the continuing considerations, it being assumed that the time profile of cdi(t) leads to a change of cbi(t), and the measuring time is conditional upon a sufficient mixture in the blood of the patient.

Equation (7) can be evaluated in widely varying forms. If one assumes cdi(t)=const, as well as cdo(t)≈const and cbi(t)≈const during the measuring phase, which is well fulfilled for the case of a concentration gradient, changing only insignificantly during the measuring time, between the two fluids (i.e. the numerator in (7) changes only insignificantly), then applicable for the period of time t to t+Δt is:

$$V(t) = \frac{\left(Qd * cdi(t) - (Qd + Qf) * cdo(t) + Qf * cbi(t)\right)\Delta t}{cbi(t + \Delta t) - cbi(t)} \qquad (8)$$

The physical or chemical characteristic of the dialyzing fluid upstream of the dialyzer is preferably increased abruptly from an original value to a predefined value, to then be abruptly reduced to a predefined value, whereupon the original value is set again. If the value by which the characteristic is reduced is twice as large as the value by which the characteristic is increased, and the time interval in which the characteristic is increased is

376269

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equal to the time interval in which the characteristic is reduced, then a symmetrical time profile is present which simplifies the evaluation, since the increase in the characteristic is offset by its decrease. In order not to have to feed to or remove from the patient unnecessary amounts of, for example, sodium during the treatment, the initial value of the characteristic in the dialyzing fluid, which is altered during the measurement, should correspond to the value in the blood.

In the event of unsymmetrical pulses for the two rectangular profiles, the change of the concentration in the blood as a function of time can be exactly calculated by forming a relationship between integral surfaces.

Determining the distribution volume is advantageously even further simplified because during the measurement, the volume of the dialyzing fluid flowing into the dialyzer is equal to the volume of fluid flowing out of the dialyzer. This can be accomplished using the familiar balancing devices. However, it is also possible to ascertain the distribution volume during a continuing ultrafiltration of the blood.

The distribution volume of a blood component in the body of an organism can then also be determined without explicitly ascertaining the change in the concentration of the component in the blood as a function of time.

An exemplary embodiment of a hemodialysis device having an apparatus for determining the urea distribution volume is further described in the following with reference to the drawing, in which:

Figure 1   shows a simplified schematic representation of
            a hemodialysis device having the apparatus for
            determining the urea distribution volume; and

5   Figure 2   shows the time profile of the dialyzing-fluid
            input and output concentration.

The apparatus for determining the urea distribution
volume can form a separate subassembly. However, it can
10   also be a component of a hemodialysis device,
particularly since some components of the apparatus for
determining the urea distribution volume are already
present in the known dialyzers. In the following, the
apparatus for determining the urea distribution volume is
15   described together with the essential components of the
dialyzer.

The hemodialysis device has a dialyzer 1 which is
separated by a semi-permeable membrane 2 into a blood
20   chamber 3 and a dialyzing-fluid chamber 4. The inlet of
the blood chamber is connected to one end of a blood feed
line 5 into which a blood pump 6 is switched, while the
outlet of blood chamber 3 is connected to the one end of
a blood discharge line 7 into which a drip chamber 8 is
25   switched.

The dialyzing-fluid system of the hemodialysis device
includes a device 9 for preparing the dialyzing fluid,
with which different compositions of the dialyzing fluid
30   (electrolyte dose) can be preselected. Preparation device
9 has a device 17 for altering the substance
concentration of the dialyzing fluid, preferably the
sodium concentration. A balancing device is also provided
which includes two parallel-connected balance chambers

that are each subdivided into two balance-chamber halves.
For the sake of greater clarity, only the two
balance-chamber halves of one balance chamber are shown
here. Preparation device 9 is connected to the inlet of
first chamber half 11a of balancing device 11 via first
section 10a of a dialyzing-fluid feed line 10. Second
section 10b of dialyzing-fluid feed line 10 connects the
outlet of first balancing-chamber half 11a to the inlet
of dialyzing-fluid chamber 4. The outlet of
dialyzing-fluid chamber 4 is connected via first section
12a of a dialyzing-fluid discharge line 12 to the inlet
of second balancing-chamber half 11b. A dialyzing-fluid
pump 13 is switched into first section 12a of
dialyzing-fluid discharge line 12. The outlet of second
balancing-chamber half 11b is connected to a drain 14 via
second section 12b of dialyzing-fluid discharge line 12.
Upstream of dialyzing-fluid pump 13, an ultrafiltrate
line 15 branches off from dialyzing-fluid discharge line
12 and likewise leads to drain 14. An ultrafiltration
pump 16 is switched into ultrafiltrate line 15.

The hemodialysis device also includes a central control
unit 18 that is connected via control lines 19 through 22
to blood pump 6, dialyzing-fluid pump 13, ultrafiltration
pump 16 and device 17 for altering the sodium
concentration of the dialyzing fluid.

During the dialysis treatment, the blood of the patient
flows through blood chamber 3,and the dialyzing fluid
flows through dialyzing-fluid chamber 4 of dialyzer 1.
Since balancing device 11 is switched into the
dialyzing-fluid path, only so much dialyzing fluid can
flow in via dialyzing-fluid feed line 10 as can flow off
via dialyzing-fluid discharge line 12. Fluid can be

withdrawn from the patient using ultrafiltration pump 16, the desired ultrafiltration rate being predetermined by the control unit.

5   Measuring devices 23, 24, respectively, are arranged in feed line 10 and discharge line 12 upstream and downstream of dialyzer 1 for determining the substance concentration of the dialyzing fluid at the input of dialyzer 1 (dialyzing-fluid input concentration cdi) and
10   the substance concentration of the dialyzing fluid at the output of the dialyzer (dialyzing-fluid output concentration cdo). Measuring devices 23, 24 for determining the dialyzing-fluid input and output concentration have conductivity sensors which preferably
15   measure the temperature-corrected conductivity of the dialyzing fluid and thus especially the Na concentration. Instead of conductivity sensors, optical or other sensors, e.g. enzyme sensors, can also be arranged in the dialyzing-fluid path for measuring the dialyzing-fluid
20   input and output concentration.

Arithmetic and evaluation unit 29 is connected via a data line 32 to control unit 18 in order to be able to retrieve flow rates Qb, Qd for blood and dialyzing-fluid
25   pumps 6, 13.

Measuring devices 23, 24 are connected via data lines 25, 26 to a memory unit 27. Memory unit 27 receives the measured values of sensors and stores them in
30   chronological sequence. The measured values are supplied via a data line 28 to an arithmetic and evaluation unit 29 which, in a digital computer (microprocessor), determines the urea distribution volume from the data obtained. The urea distribution volume is displayed on a

readout mechanism 30 that is connected via a data line 31
to arithmetic and evaluation unit 29.

The apparatus operates as follows for determining the
urea distribution volume:

At the beginning of the measurement, control unit 18
halts ultrafiltration pump 16, so that the
ultrafiltration rate is equal to 0. The control unit
predefines flow rates Qb and Qd for the flow of the blood
and dialyzing fluid.

The dialyzing fluid flows through the dialyzing-fluid
chamber with a flow rate Qd predefined by the speed of
pump 13, and with dialyzing-fluid input concentration cdi
which is set by device 17 and which is detected by
measuring device 23 arranged upstream of the dialyzer.
The dialyzing-fluid output concentration cdo appearing in
response to the dialysis is detected by measuring device
24 arranged downstream of the dialyzer.

Device 17 adjusts a dialyzing-fluid input concentration
$cdi(t)$ which has the time profile shown in Figure 2.
Starting from a value cdi_0 which is customary for the
dialysis treatment and which corresponds or at least
comes close to the value cbi_0 of the sodium concentration
in the blood upstream of the dialyzer, the input
concentration is increased to the value cdi_1 at point of
time t_0. At point of time t_1, the input concentration is
reduced to the value cdi_2, to then be set again to the
original value cdi_0 at point of time t_2.

Figure 2 shows, in dotted lines, the time profile of
dialyzing-fluid output concentration $cdo(t)$ appearing

downstream of the dialyzer. $cdi_0 = cdo_0$ is for $t < t_0$. At
the end of time interval $t_0 < t < t_1$, a value cdo_1 appears
at the dialyzer output, while at the end of time interval
$t_1 < t < t_2$, a value cd_{o2} appears at the dialyzer output.

5   For $t > t_2$, the dialyzing-fluid output concentration again
assumes the value of the dialyzing-fluid input
concentration with sufficient accuracy.
The dialyzing-fluid input and output concentrations
exhibit a symmetrical time profile. The value by which

10   the input concentration is reduced is twice as large as
the value by which the input concentration is increased.
Time interval $t_1 - t_0$ is equal to time interval $t_2 - t_1$.
The time intervals are regulated such that in each case
stable values ensue for cdo. Since the profile is

15   symmetrical, the shift of electrolytes via the membrane
of the dialyzer, caused by the first change, is
compensated for again.

While the dialyzing-fluid input concentration is changed,

20   the dialyzing-fluid input and output concentrations cdi_0,
cdo_0 within time interval $t < t_0$, cdi_1, cdo_1 within time
interval $t_0 < t < t_1$ and cdi_2, cdo_2 within time interval
$t_1 < t < t_2$ are measured and stored in memory unit 27. In
so doing, it is taken into account that the values for

25   cdo are time-displaced by a delay time t_d with respect to
those of cdi.

Since the shift of electrolytes via the dialysis
membrane, caused by the first change, is compensated for

30   again in the symmetrical case, the following applies:

$$cdi_0 = cbi_0 = cbi_2 \qquad\qquad (9)$$

points of time immediately prior to the change of cdi being designated in each case with the subscript as t_0, t_1 and t_2.

5   The change as a function of time in the blood-input concentration Δcbi is calculated as follows:

$$\Delta cbi = cbi_1 - cbi_0 \qquad (10)$$

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On condition that an ultra-filtration rate of zero (Qf=0) is set, and assuming that dialysance D does not change during the measurement, arithmetic and evaluation unit 29
15   calculates Δcbi from the stored values cdi_0, cdo_0, cdi_1, cdo_1 and cdi_2, cdo_2, as well as from the adjusted dialyzing-fluid flow rate Qd on the basis of the following equations:

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$$D = \frac{[(cdo_0 - cdi_0) - (cdo_1 - cdi_1)]Qd}{(cbi_0 - cdi_0) - (cbi_1 - cdi_1)} \qquad (11)$$

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$$D = \frac{[(cdo_1 - cdi_1) - (cdo_2 - cdi_2)]Qd}{(cbi_1 - cdi_1) - (cbi_2 - cdi_2)} \qquad (12)$$

$$D = \frac{[(cdo_0 - cdi_0) - (cdo_2 - cdi_2)]Qd}{(cbi_0 - cdi_0) - (cbi_2 - cdi_2)} \qquad (13)$$

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35   In these three equations, only D and Δcbi are unknown.

The arithmetic unit ascertains these parameters either
from two equations hereof, from average values of the
respective combinations in pairs, or from a variation
calculation which tries to fulfill all three equations as
well as possible. In the event D is already known, this
can be utilized for further optimization.

After D and Δcbi are ascertained, sodium distribution
volume V is calculated in the arithmetic unit according
to equation (8), where $\Delta cbi=cbi(t+\Delta t)-cbi(t)$ and $\Delta t=t_1-t_2$.

For this purpose, arithmetic and evaluation unit 29 reads
out the measured values for the dialyzing-fluid input and
output concentrations $cdi(t)$, $cdo(t)$, stored during the
measurement in their chronological sequence, from memory
unit 27. The measuring signals of the conductivity
sensors are advantageously sampled, the calculation being
carried out by a digital computer.

Assuming that the ascertained sodium distribution volume
is essentially equal to the urea distribution volume, the
urea distribution volume is determined and displayed on
readout mechanism 30. From the known clearance K and
treatment time t and the ascertained urea distribution
volume V, arithmetic and evaluation unit 29 calculates
the "Kt/V" parameter which quantifies the dialyzing
dosage. The "Kt/V" parameter is likewise displayed on
readout mechanism 30.

For the aforesaid reasons, the change in the
dialyzing-fluid input concentration as a function of time
should be symmetrical. However, if unsymmetrical pulses
are used, it can no longer be assumed that $cbi_0 = cbi_2$.
Applicable in this case is:

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$$cbi_2 = cbi_0 + \Delta cbi\left(I_1 + I_2\right) / I_1 \qquad (14)$$

$$I_1 = \int_0^{t_1} \left[cdi(t) - cdo(t + td)\right] dt \qquad (15)$$

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$$I_2 = -\int_{t_1}^{t_2} \left[cdi(t) - cdo(t + td)\right] dt \qquad (16)$$

Delay time td is the time after which the dialyzing-fluid
output concentration rises after the increase of the
10 dialyzing-fluid input concentration. Delay time td is
calculated from the measured time profile of input and
output concentrations cdi(t) and cdo(t). It is evident
from Figure 2 that, for the case of a symmetrical profile
of cdi, integral surfaces I_1 and I_2 are nearly identical,
15 which means, as assumed before,
cbi_2 = cbi_0.

The sodium distribution volume is again calculated in
arithmetic and evaluation unit 29 according to the
20 equations (11) through (13), now, however,
cbi_2 = cbi_0 + $\Delta cbi(I_1 + I_2)/I_1$ being valid. The arithmetic
and evaluation unit is provided with integrators for
forming integrals I_1 and I_2.

25 If ultrafiltration is carried on during the measurement,
the sodium distribution volume can only be determined
when the values $cbi_{0,1,2}$ for the blood input concentration
are known.

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376269   18

To this end, prior to measuring the distribution volume, the blood input concentration cbi can be determined as described in detail in the German patent 39 38 662 C2, to which reference is specifically made. In this context, it is sufficient to ascertain an average value for $cbi_{0,1,2}$.

Arithmetic and evaluation unit 29 now determines Δcbi on the basis of the following equations:

$$D_{diff} = \frac{\left[(cdo_0 - cdi_0) - (cdo_1 - cdi_1)\right]Qd + \left[(cbi_1 - cdo_1) - (cbi_0 - cdo_0)\right]Qf}{\left(1 - \frac{Qf}{Qb}\right)\left[(cbi_0 - cdi_0) - (cbi_1 - cdi_1)\right]} \quad (17)$$

$$D_{diff} = \frac{\left[(cdo_1 - cdi_1) - (cdo_2 - cdi_2)\right]Qd + \left[(cbi_2 - cdo_2) - (cbi_1 - cdo_1)\right]Qf}{\left(1 - \frac{Qf}{Qb}\right)\left[(cbi_1 - cdi_1) - (cbi_2 - cdi_2)\right]} \quad (18)$$

$$D_{diff} = \frac{\left[(cdo_0 - cdi_0) - (cdo_2 - cdi_2)\right]Qd + \left[(cbi_2 - cdo_2) - (cbi_0 - cdo_0)\right]Qf}{\left(1 - \frac{Qf}{Qb}\right)\left[(cbi_0 - cdi_0) - (cbi_2 - cdi_2)\right]} \quad (19)$$

D_{diff} represents the diffusive component of the dialysance.

The change as a function of time in the blood-input concentration Δcbi is now determined in a similar manner as in the case of $Q_f = 0$ from equations (17) through (19). The sodium distribution volume is then in turn calculated according to equation (8). Arithmetic and evaluation unit 29 thereupon again determines the urea distribution volume from the sodium distribution volume.

376269   19

However, distribution volume V of a blood component in the body of an organism can also be determined in arithmetic and evaluation unit 29 without explicitly ascertaining the change as a function of time in the concentration of the component in the blood Δcbi. To this end, device 17 again sets the profile, shown in Figure 2, for the dialyzing-fluid input concentration $cdi(t)$. The points of time "beginning", "end of the high phase" and "end of the low phase" are again indexed with 0, 1 and 2, respectively.

Dialysance D can be calculated as follows from the dialyzing-fluid input and output concentrations at points of time i, j:

$$D_{i,j} = \left(1 - \frac{cdo_i - cdo_j}{cdi_i - cdi_j}\right)(Qd + Qf) \quad \text{time index } i \neq j \tag{20}$$

The above equation is derived assuming that the plasma-sodium is constant. However, this is not the case because of the salt transfer. If this assumption is not made, then the dialysance is calculated as follows:

$$D_{i,j} = \frac{\left[(cdo_i - cdi_i) - (cdo_j - cdi_j)\right]Qd + \left[(cbi_j - cdo_j) - (cbi_i - cdo_i)\right]Qf}{(cbi_i - cdi_i) - (cbi_j - cdi_j)} + Qf \tag{21}$$

Analogously, the diffusive component of dialysance D_{diff} for a constant plasma-sodium concentration reads as follows:

$$D_{diff\,i,j} = \frac{\left[(cdo_i - cdi_i) - (cdo_j - cdi_j)\right]Qd + (cdo_i - cdo_j)Qf}{\left(1 - \frac{Qf}{Qb}\right)\left[(cdi_j - cdi_i)\right]} \tag{22}$$

376269   20

If the assumption is dropped, the diffusive component of dialysance D_{diff} is calculated as follows:

$$D_{diff\,i,j} = \frac{\left[\left(cdo_i - cdi_i\right) - \left(cdo_j - cdi_j\right)\right]Qd + \left[\left(cbi_j - cdo_j\right) - \left(cbi_i - cdo_i\right)\right]Qf}{\left(1 - \frac{Qf}{Qb}\right)\left[\left(cbi_i - cdi_i\right) - \left(cbi_j - cdi_j\right)\right]} \qquad (23)$$

Experiments have shown that, for the step-index profile shown in Figure 2, equations (20) and (22), respectively, are a good approximation for equations (21) and (23), respectively, for i=1 and j=2.

If the values for the dialysance, which take into account the electrolyte transfer, are now compared to those resulting from a constant blood input concentration cbi, then distribution volume V can be determined.

To determine the distribution volume V, arithmetic and evaluation unit 29 first of all calculates, from the stored measured values, values $D_{0,1}$, $D_{1,2}$ and $D_{diff1,2}$ according to equations (20) and (22) for dialysance D and the diffusive component of the dialysance D_{diff}. An ultra-filtration rate Qf of zero is preferably set when acquiring the measurable quantities cdi and cdo.

After determining the above values, the arithmetic and evaluation unit then calculates the distribution volume of the blood component according to the following equation:

$$V(t_1) = \left(\frac{D_{0,1}}{D_{1,2} - D_{0,1}} + 1\right) \bullet \left(\frac{D_{diff\,1,2}(t_1 - t_0)(cdi_1 - cbi_0)}{cdi_1 - cdi_0}\right) \qquad (24)$$

For a constant ultrafiltration rate, distribution volume V can be calculated for any points of time t as follows:

$$V(t) = V(t_1) + Qf \; (t_1 - 1)$$

The concentration of the component in the blood cbi_0 (blood-input concentration) is determined beforehand according to equation (4a) or (4b). Namely, after the arithmetic and evaluation unit has determined the dialysance, the sought-after concentration cbi is the single unknown.

The above equations show that it is not explicitly necessary to determine the change in the blood-input concentration as a function of time. It is sufficient to determine this variable at point of time t_0.

Equation (24) was derived assuming that the measurable quantities are recorded only a few minutes after a change in the dialyzing-fluid input concentration, and a shift of electrolytes through the dialyzer membrane proportional to the time ensues. It was further assumed that the recirculation in the fistula of the patient can be disregarded. To expand the validity range as a function of time and to take into account the recirculation, it is also possible to allow for empirically ascertained correction factors a_1 for $D_{0,1}$, $D_{1,2}$ and $D_{diff1,2}$ in equation (24). The calculation is then carried out according to the following equation:

$$V(t_1) = \left(\frac{a_1 D_{0,1}}{a_2 D_{1,2} - a_1 D_{0,1}} + 1 \right) \bullet \left(\frac{a_3 D_{diff\,1,2}(t_1 - t_0)(cdi_1 - a_4 cbi_0)}{cdi_1 - cdi_0} \right) \qquad (25)$$

Experiments have shown that the measuring accuracy is high particularly when the blood and dialyzing-fluid flow Qb, Qd are high.

5

10